

**What is claimed:**

1. A biological sensor comprising:  
a porous semiconductor structure comprising a central layer  
5 interposed between upper and lower layers, each of the upper and lower layers  
including strata of alternating porosity; and  
one or more probes coupled to the porous semiconductor  
structure, the one or more probes binding to a target molecule, whereby a detectable  
change occurs in a refractive index of the biological sensor upon binding of the one or  
10 more probes to the target molecule.
2. The biological sensor according to claim 1 wherein the central  
active layer has a porosity of about 50 to about 90 percent.
- 15 3. The biological sensor according to claim 2 wherein the central  
active layer has a porosity of about 65 to about 85 percent.
4. The biological sensor according to claim 1 wherein each of the  
upper and lower layers comprise six or more strata of alternating porosity.
- 20 5. The biological sensor according to claim 1 wherein the strata of  
alternating porosity comprise first stratum having a porosity of about 35 to about 70  
percent and second stratum having a porosity greater than the porosity of the first  
stratum.
- 25 6. The biological sensor according to claim 1 wherein the porous  
semiconductor structure comprises pores with an average pore size of between about 2  
nm to about 2000 nm.
- 30 7. The biological sensor according to claim 1 wherein the porous  
semiconductor structure comprises pores with an average pore size of between about  
10 nm to about 100 nm.

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8. The biological sensor according to claim 1 wherein the probe is a non-polymeric small molecule selected from the group consisting of avidin, peptidomimetic compounds, and vancomycin.

5 9. The biological sensor according to claim 1 wherein the probe is a tetratryptophan *ter*-cyclopentane which binds to lipopolysaccharide.

10 10. The biological sensor according to claim 1 wherein the probe is a polypeptide selected from the group consisting of a receptor for cell surface molecule, a lipid A receptor, an antibody or fragment thereof, a peptide monobody, a lipopolysacchardide-binding polypeptide, a peptidoglycan-binding polypeptide, a carbohydrate-binding polypeptide, a phosphate-binding polypeptide, a nucleic acid-binding polypeptide, and a polypeptide which binds an organic warfare agent.

15 11. The biological sensor according to claim 1 wherein the probe is a nucleic acid molecule.

20 12. The biological sensor according to claim 1 further comprising:  
one or more coupling agents each comprising a first moiety attached to the porous semiconductor structure and a second moiety which binds to the probe.

25 13. The biological sensor according to claim 12 wherein the one or more coupling agents are silanes.

30 14. The biological sensor according to claim 13 wherein the silanes are selected from the group consisting of 3-glycidoxypropyltrialkoxysilanes with C1-6 alkoxy groups, trialkoxy(oxiranylalkyl)silanes with C2-12 alkyl groups and C1-6 alkoxy groups, 2-(1,2-epoxycyclohexyl)ethyltrialkoxysilane with C1-6 alkoxy groups, 3-butenyl trialkoxysilanes with C1-6 alkoxy groups, alkenyltrialkoxysilanes with C2-12 alkenyl groups and C1-6 alkoxy groups, tris[(1-methylethenyl)oxy]3-oxiranylalkyl silanes with C2-12 alkyl groups, [5-(3,3-dimethyloxiranyl)-3-methyl-2-pentenyl]trialkoxysilane with C1-6 alkoxy groups, (2,3-oxiranediyl)di-2,1-ethanediyl)bis-triethoxysilane, trialkoxy[2-(3-methyloxiranyl)alkyl]silane with C1-6

alkoxy groups and C2-12 alkyl groups, trimethoxy[2-[3-(17,17,17-trifluoroheptadecyl)oxiranyl]ethyl]silane, tributoxy[3-[3-(chloromethyl)oxiranyl]-2-methylpropyl]silane, and combinations thereof.

5            15.        The biological sensor according to claim 12 wherein each of the one or more probes comprises a plurality of binding sites, at least one of which binds to the target and at least one of which is bonded to the second moiety of the coupling agent.

10            16. The biological sensor according to claim 15 wherein the plurality of binding sites on the probe are the same, the biological sensor further comprising:

a plurality of blocking agents, each bonded to the second moiety of the coupling agent under conditions effective to preclude all of the plurality

15 of binding sites on a single probe from binding to the second moieties on the one or more coupling agents.

17. The biological sensor according to claim 16 wherein the plurality of blocking agents are amino acid alkyl esters.

20 18. The biological sensor according to claim 1 wherein the one or more probes are the same.

19. The biological sensor according to claim 1 wherein the one or  
25 more probes are coupled to the porous semiconductor structure throughout the central  
layer and the upper and lower layers.

20. The biological sensor according to claim 1 wherein the one or more probes comprises two or more probes which are different, each binding to different target molecules.

21. The biological sensor according to claim 19 wherein the porous semiconductor structure includes at least two zones, one of the two or more probes being bonded to the porous semiconductor structure within a first zone and another of

the two or more probes being bonded to the porous semiconductor structure within a second zone.

22. A method of making a biological sensor which detects a target molecule, the method comprising:
- providing a primed porous semiconductor structure including a central layer interposed between upper and lower layers, each of the upper and lower layers including strata of alternating porosity, and a coupling agent bound to the semiconductor structure; and
- exposing the primed porous semiconductor structure to a probe molecule including (i) one or more semiconductor structure-binding groups and (ii) one or more target-binding groups that bind to a target molecule, said exposing being carried out under conditions effective to bind the probe molecule to the primed porous semiconductor structure via the coupling agent or directly to the semiconductor structure upon displacement of the coupling agent, with the one or more target-binding groups remaining available for binding to the target molecule.

23. The method according to claim 22 wherein the probe is a non-polymeric small molecule, a protein or polypeptide, or a nucleic acid.

24. The method according to claim 22 wherein the target-binding group is an amino group, a thiol, a hydroxyl, an alkyl chain, an ester, a carboxylic acid, an aromatic, or a heterocycle.

25. The method according to claim 22 wherein the semiconductor structure-binding group is an amino group, a thiol, a hydroxyl, an alkenyl.

26. The method according to claim 22 wherein the coupling agent is an epoxide, a halo, a thiol, or an alkenyl.

27. The method according to claim 22 wherein the probe molecule covalently binds to the coupling agent during said exposing.

28. The method according to claim 22 wherein the probe molecule covalently binds to the porous semiconductor structure upon displacement of the coupling agent.

5 29. The method according to claim 22 wherein said providing a primed porous semiconductor structure comprises:

providing a coupling agent precursor which binds to the semiconductor and

10 exposing a porous semiconductor structure, comprising a central layer interposed between upper and lower layers, each of the upper and lower layers including strata of alternating porosity, to the coupling agent under conditions effective to form the primed porous semiconductor structure.

15 30. The method according to claim 29, wherein said providing a primed porous semiconductor structure further comprises:

preparing the porous semiconductor structure.

20 31. The method according to claim 22 further comprising:  
exposing the primed porous semiconductor structure to a blocking agent.

32. The method according to claim 31 wherein said exposing the primed porous semiconductor structure to a blocking agent is carried out prior to said exposing the porous semiconductor structure to a probe molecule.

25 33. The method according to claim 31 wherein said exposing the primed porous semiconductor structure to a blocking agent is carried out simultaneously with said exposing the porous semiconductor structure to a probe molecule.

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34. A detection device comprising:  
a biological sensor according to claim 1;  
a source of illumination positioned to illuminate the biological  
sensor; and

5 a detector positioned to capture photoluminescent emissions  
from the biological sensor and to detect changes in photoluminescent emissions from  
the biological sensor.

35. A method of detecting a target molecule comprising:  
10 exposing a biological sensor according to claim 1 to a sample  
under conditions effective to allow binding of a target molecule in the sample to the  
one or more probes of the biological sensor; and

determining whether the biological sensor emits a  
photoluminescent emission pattern which shifts following said exposing, whereby a  
15 shifted photoluminescent emission pattern indicates the presence of the target  
molecule in the sample.

36. The method according to claim 35 wherein said determining  
comprises:

20 measuring a first photoluminescent emission pattern prior to  
said exposing;

measuring a second photoluminescent emission pattern after  
said exposing; and

25 comparing the first and second photoluminescent emission  
patterns.

37. The method according to claim 35 wherein said measuring is  
carried out using a light source and a spectral analyzer.

30 38. The method according to claim 35 wherein the target molecule  
is a protein, glycoprotein, peptidoglycan, carbohydrate, lipoprotein, lipoteichoic acid,  
lipid A, phosphate, nucleic acid, or organic compound.

39. A method of detecting the presence of Gram negative bacteria in a sample comprising:

exposing a sample to a biological sensor comprising (i) a porous photoluminescent semiconductor structure comprising a central layer interposed between upper and lower layers, each upper and lower layer including strata of alternating porosity and (ii) one or more probes coupled to the porous photoluminescent semiconductor structure, the one or more probes binding to lipid A or fragments thereof; and

determining whether the biological sensor emits a photoluminescent emission pattern which shifts following said exposing, whereby a shifted photoluminescent emission pattern indicates the presence of lipid A and, thus, Gram negative bacteria in the sample.

40. The method according to claim 39 wherein said determining comprises:

measuring a first photoluminescent emission pattern prior to said exposing;

measuring a second photoluminescent emission pattern after said exposing; and

comparing the first and second photoluminescent emission patterns.

41. The method according to claim 40 wherein each said measuring is carried out using a light source and a detector.

42. The method according to claim 39 wherein the sample is blood, water, a suspension of solids in an aqueous solution, or a tissue homogenate.

43. The method according to claim 42, wherein the solids suspended in the aqueous solution are food particles, soil particles, or a cell suspension from a clinical isolate.

44. The method according to claim 39 further comprising:  
treating the sample prior to said exposing in a manner effective  
to disrupt the cellular membrane of Gram negative bacteria in the sample.

5 45. The method according to claim 44 wherein said treating  
comprises chemical treatment, mechanical treatment, sonication, or freezing.

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